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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/872,349	05/31/2001	Sidney Pestka	PBLI-P01-007	1152
28120	7590	09/13/2004	EXAMINER	
ROPES & GRAY LLP ONE INTERNATIONAL PLACE BOSTON, MA 02110-2624			HELMS, LARRY RONALD	
			ART UNIT	PAPER NUMBER

1642

DATE MAILED: 09/13/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/872,349	PRESTKA	
	Examiner	Art Unit	
	Larry R. Helms	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE ____ MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☐ Claim(s) ____ is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☐ Claim(s) ____ is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|-----------------------------------------------------------------------------------------|-----------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. ____. |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date ____. | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

1. Claims 33, 41-42 have been amended.
Claim 34 has been canceled.
2. Claims 33, 35-42 are pending and under examination.
3. The text of those sections of Title 35 U.S.C. code not included in this office action can be found in a prior Office Action.
4. The following Office Action contains NEW GROUNDS of rejection.

Rejections Withdrawn

4. The rejection of claims 33-42 under 35 U.S.C. 112, second paragraph, as indicated in paragraph 4, parts B-E in the previous Office Action, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the amendments to the claims.
5. The rejection of claims 33-34, 37, 39-41 under 35 U.S.C. 102(b) as being anticipated by Lin et al (Anticancer Res 18:3971-78, 1998) is withdrawn in view of the amendments to the claims.
6. The rejection of claims 33-34, 37-42 under 35 U.S.C. 103(a) as being unpatentable over Lin et al (Anticancer Research 18:3971-78, 1998), as applied to claims 33-34, 37, 39-41 above, and further in view of Pestka (US Patent 5,986,061, filed 6/95) is withdrawn in view of the amendments to the claims.

Response to Arguments

7. The rejection of Claims 33, 35-42 under 35 U.S.C. 112, second paragraph, under paragraph 4, part A in the previous Office Action, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained.

The response filed 6/24/04 has been carefully considered but is deemed not to be persuasive. The response states that claim 33 has been amended to recite "in vitro", thereby rendering the rejection moot (see page 4 of response). In response to this argument, adding "in vitro" does not overcome the rejection because it is still unclear what the conditions are for the in vitro incubation and different conditions can influence the attached groups. As previously stated, "What is the temperature? Is there a preincubation time?", in addition what are the full set of conditions.

8. The rejection of claims 33, 35-42 are rejected under 35 U.S.C. 112, first paragraph, is maintained.

The response filed 6/24/04 has been carefully considered but is deemed not to be persuasive. The response states that it appears that the examiner is conceding that the specification is enabling for antibodies that do bind antigen and wherein the phosphate group remains after incubation in vitro and as such the claims have been amended to recite that the kinase site does not adversely affect binding and the incubation is in vitro (see page 5 of response). In response to this argument, the rejection was in the form of a scope rejection which was stated previously "while being

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enabling for an antibody that binds antigen that is engineered to contain a serine at position 224 or a kinase recognition site at the carboxyl terminus in the linear amino acid sequence in the constant region wherein at least 80% of the phosphate groups remains attached after 36 hours in serum or buffer in vitro". Thus adding only that the antibody binds antigen and is incubated in vitro only satisfies part of the enablement rejection. The claims are only enabled for a kinase site at position 224 or at the C-terminus in the linear amino acid sequence. The claims have been amended to recite the kinase site is in the hinge region, but the claims still encompass the kinase site at other places in the hinge other than position 224 or other than SER at position 224. The specification does not enable antibodies with a kinase site other than position 224 with the claimed properties as stated in the rejection "The specification teaches that structural distortions may result from the attachment of phosphate groups to antibodies (see page 64) and it is extremely difficult to get the crystal structure of an intact antibody (see page 62, line 25) and the phosphoserine at position 224 in the new constructs is highly resistant to hydrolysis (see page 64, lines 25-26). The specification teaches constructs which all have SER224 as the kinase recognition site (see Table 1) and the molecules were stable in serum or buffer in vitro for 5-21 days (see Table 5) and the specification discloses that MAb-WW5 which has SER 224 had a biodistribution that was higher in tumors than in other tissue or blood after 168 hours in a mouse in vivo tumor model (see Table 9). The specification teaches that there was significant hydrolysis of the phosphate from Mab-chCC49K1 where the fusion was at the C-terminus and that the molecule MAb-chCC49-6P was 91-93% stable after 36 hours in

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serum or buffer in vitro (see page 64, lines 22-24 and Table 3). The specification does not enable any other kinase site other than SER 224 or other than at a C-terminus of the linear amino acid sequence in a heavy chain or engineering any site that is protected from hydrolysis by the interaction with other amino acids or any molecule that is stable for at least 5 days in vivo.". In addition the response does not address the concerns of the time of incubation or percentages of the phosphorylated form at the time of incubation or the detection of intermolecular interactions as was addressed in the rejection as evidenced from the disclosure in the specification and the art of Harris and Lin. For these reasons the rejection is maintained.

The following is a NEW GROUND of rejection

Claim Rejections - 35 USC § 112

4. Claims 33, 35-42 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

a. Claims 33, 35-42 are indefinite for reciting "does not adversely affect the ability of the antibody...to bind antigen" in claim 33 because the term "adversely" is a relative term. Does the antibody retain full binding or only partial binding or does the phrase "does not adversely affect the ability" mean the antibody's affinity is the same or similar to the unmodified antibody?

Conclusion

9. No claims are allowed.

10. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Larry R. Helms, Ph.D, whose telephone number is (571) 272-0832. The examiner can normally be reached on Monday through Friday from 6:30 am to 4:00 pm, with alternate Fridays off. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffery Siew, can be reached at (571) 272-0787.


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12. Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The Fax Center telephone number is 703-872-9306.

Respectfully,

Larry R. Helms Ph.D.

571-272-0832



LARRY R. HELMS, PH.D
PRIMARY EXAMINER